tongue of a mammal [The cells of claim 24], or neurons, astrocytes or oligodendrocytes differentiated from said isolated precursor [the] cells [of claim 24, in a kit for the treatment of a disease, disorder, or abnormal physical state comprising neurodegenerative disease or neurotrauma].

REMARKS

Summary of the Invention

The invention features isolated precursor cells, and methods, kits, and compositions that include these cells.

Support for the Amendments

Claims 9, 10 and 28 have been amended to clarify that the claimed cells are differentiated cells. Support for these amendments is found at page 8, lines 8-14 of the specification. Claim 22 has been amended to clarify that the claim is to a method of using isolated precursor cells for toxicity testing of a substance, testing drug efficacy, derivation of cell lines, and isolation of proteins. Support for this amendment is found at page 10, line 19 to page 11, line 8 of the specification. Claims 8, 11, 21, 27, 28, and 29 have been amended such that the claims have proper dependency. No new matter has been added with these amendments.

Summary of the Office Action

Claim 28 is objected to under 37 CFR § 1.75(c). Claims 11, 21-23, 29, and 30 stand rejected under 35 U.S.C. § 112, first paragraph. Claim 22 stands rejected under 35 U.S.C. § 112, second paragraph. Claims 1-5, 7-11, and 21-23 stand rejected under 35 U.S.C. § 102(b). Claim 6 stands rejected under 35 U.S.C. § 103(a).

Rejections under 37 CFR § 1.75(c)

Claim 28 stands objected to under 37 CFR 1.75(c) as being of improper dependent form. This objection has been overcome by amendment to claim 28, which is now dependent on claim 27.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 11, 21-23, 29, and 30 are rejected for containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make or use the invention. This rejection has been met by amendment of claims 11, 21, 22, and 29, cancellation of claims 23 and 30, and the following remarks.

Claim 22, as amended, recites a method of using the isolated precursor cells (or cells differentiated from these precursor cells) for "toxicity testing of a substance" At page 10, lines 22-25, of the specification, this is described as follows:

> Toxicity testing is done by culturing precursor cells or cells differentiated from precursor cells in a suitable medium and introducing a substance, such as a pharmaceutical or chemical, to the culture. the precursor cells or differentiated cells are examined to determine if the substance has had an adverse effect on the culture.

These cells can be used in any number of cytotoxicity tests and their broad applicability in toxicity testing would be clear to those skilled in the art. This rejection can now be removed.

Rejections under 35 U.S.C. § 112, second paragraph

Claim 22 is rejected for indefiniteness. The Examiner stated that the phrase "testing toxicity" is unclear. This rejection has been overcome by the amendment of claim 22, described above, to specify that the toxicity testing is testing of a substance. The rejection of claim 22 for indefiniteness can now be removed.

Rejections under 35 U.S.C. § 102(b)

Calof

Claims 1-5, 7-11, and 21-23 stand rejected under 35 U.S.C. §102(b) as being anticipated by Calof et al., Neuron 3:315-327, 1989 (hereafter "Calof"). This rejection is respectfully traversed.

Claim 1 recites "isolated precursor cells from an olfactory epithelium of a

mammal." The remaining rejected claims are dependent on claim 1. The term "isolated" refers to the fact that all cell types other than the precursor cells have been removed by killing (see, for example, page 16, lines 14-16, and page 20, lines 8-9, of the specification). The use of the word "isolated" in this respect is consistent with the definition of "isolated" as being "pure; not combined" (Webster's New Universal Unabridged Dictionary, 2nd Edition).

The Examiner states that Calof discloses isolated precursor cells from the mouse olfactory epithelium. Applicants respectfully disagree. It is Applicants' position that at no time did the cultures described by Calof consist of isolated precursor cells. Table 1 (at page 319 of Calof) provides evidence that, at all times examined, at least 25% of the cultured cells were NCAM-positive neurons, which are not precursor cells. As Calof does not describe isolated precursor cells, as required in the rejected claims, the rejection in view of Calof should be withdrawn.

Mayo

Claims 24-30 stand rejected under 35 U.S.C. §102(b) as being anticipated by Mayo et al., Int. J. Dev. Biol. 36:255-263, 1992 (hereafter "Mayo"). This rejection is respectfully traversed.

Claim 24 recites "isolated precursor cells from a tongue of a mammal." Again, as described above, all cells other than precursor cells have been removed, resulting in a

population of isolated precursor cells.

The Examiner states that Mayo describes isolated precursor cells from a mouse tongue. Applicants respectfully disagree; at no time does Mayo describe or suggest the isolation of any cells from a tongue. The greatest percentage of any one cell type described by Mayo is "nearly 50%" (see Mayo, page 259, second column, line 16) after nine days in culture. Mayo discloses that, after these nine days, the culture system was "permissive for chondrogenesis, osteogenesis, and tooth development" (page 259, second column, lines 41-42, of the specification). Clearly, the cells of Mayo represent a heterogeneous population. Moreover, at no time does Mayo mention the presence of even one precursor cell (defined at page 7, lines 18-20, of the specification as being "neural stem cells or neural progenitor cells"). In sum, as Mayo does not disclose or suggest isolated precursor cells from a tongue, the rejection should be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claim 6 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Calof in view of Le Gal La Salle et al., Science 259:988-990, 1993 (hereafter "Le Gal La Salle"). This rejection is respectfully traversed.

Claim 6 is directed to isolated neural precursor cells from an olfactory epithelium of a mammal that have been transfected with a heterologous gene.

If one were to combine the teachings of Calof with those of Le Gal La Salle, one

would still not have Applicants' invention.

According to the Examiner, Le Gal La Salle describes infecting primary cultures of sympathetic neurons with an adenovirus encoding β-galactosidase. Le Gal La Salle does not describe isolated neural precursor cells from an olfactory epithelium of a mammal.

The Examiner is referred to the above discussion of Calof in which it is pointed out that Calof does not describe isolated neural precursor cells from an olfactory epithelium of a mammal.

As each reference fails to describe a central feature of the claim, namely isolated neural precursor cells from an olfactory epithelium of a mammal, it follows that the combination of Calof and Le Gal La Salle could not make Applicants' invention obvious. Thus, the rejection of claim 6 for obviousness should be removed.

Conclusion

Applicants hereby submit that the claims are now in condition for allowance, and such action is respectfully requested. If the claims are not deemed to be in condition for allowance, the undersigned requests a telephone interview in order to discuss the remaining rejections.

Enclosed is a petition to extend the period for replying for three months, to and including April 15, 1999. If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: April 15, 1999

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